September 19, 1958

Dr. Herman Kalckar
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Baltimore 18, Maryland

Dear Herman:

Our very best wishes to you at Johns Hopkins.

As you know we have been away most of the summer and this accounts for our unsatisfactory behavior as correspondents. Also I seemed wise to give you a chance to settle in in Baltimore.

I was very pleased to receive your last letter of September 13 with its additional information that may help to tidy up some of the connected issues in galactose metabolism. I am really snowed under this week and Esther and I want some more time to digest this and your previous correspondence before making more detailed comments. I honestly intend to write you again in a very short time. Meanwhile let me remark how pleased I am to see the quantitative data coming through per the little sketch in your letter, which helps to clarify some of the issues that were fuzzy in my mind. I thought I had recommended to you a long time ago to stay away from glucose which is a notorious inhibitor of non-glucose enzymes.

A propos the apparent selection of mutants in the galactose medium I suggest that you test these to see whether they have become lactose negative. The full mechanism for this is not apparent but we have frequently been successful in selecting lactose negative mutants as outgrowths of galactose negative cultures on galactose medium. This may be connected with the permease functions of the Lac gene, a mutation wherein would possibly inhibit the entry of galactose and therefore relieve the inhibition of growth.

I am rather surprised that you found no galactose in the polysaccharide complex. Kauffmann in Copenhagen is collaborating with Westphal on a comprehensive survey of gram negative bacteria and they have found galactose in the somatic antigen of almost all the strains they looked at. In fact their list included only one or two strains of E. coli, out of a great many, which did <u>not</u> have galactose and I have asked Kauffmann whether he would be willing to send me one of these strains. I am waiting to hear from him. I am not clear from your letter which strain you analysed: was it W 3099 or the wild type? It seems to me that would be a very worthwhile enterprise.

I imagine it would not be terribly difficult to do the cross of W 3099 x Shigella, but for my own part I think it might be even better to make some recombinants of some other strains of E. coli which can be done in a number of cases. Before undertaking this there are two items of information that we should have. First, from you, whether the wild type strain of E. coli K 12 does also contain no galactose. And then second, I will verify from Kauffmann which of the

potential fertile strains of E. coli that we might use has definitely been shown to contain galactose. Given these points there should be no serious difficulty in producing the strain you would be interested in.

I will close by merely tantalizing you with the implication that we have a number of other types of mutants that are still not of the stage of preliminary genetic investigation and you will hear further from us at the earliest possible moment suitable for discussing them.

With very best regards.